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Diagnosing and Treating Syphilis in HIV-Infected Patients

The clinical manifestations, serologic responses, efficacy of treatment, and occurrence of complications of syphilis may be altered in patients coinfected with human immunodeficiency virus (HIV). Because syphilis is a disease with a broad range of manifestations and variable course, assessing reports of unusual clinical or laboratory findings in HIV-coinfected patients is difficult (*1*). On March 21 and 22, 1988, experts* from academic medical centers and state and local health departments met at CDC to discuss the diagnosis and treatment of syphilis in HIV-infected patients. The following recommendations were developed based on these discussions.

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Diagnosis of Syphilis in HIV-Infected Patients

Most HIV-infected patients appear to have a normal serologic response to *Treponema pallidum* infection (*2*). However, in some HIV-infected patients with biopsy-confirmed secondary syphilis, both nontreponemal and treponemal tests for syphilis are negative (*3*). In addition, some patients infected with both *T. pallidum* and HIV have had unusually high titers on nontreponemal serologic tests for syphilis (CDC, unpublished data, 1987–88), possibly because of HIV-related polyclonal B-cell stimulation. The frequency of unusual clinical and laboratory manifestations of syphilis in patients coinfected with HIV is unknown.

Recommendations

1. Persons with HIV infection acquired through sexual contact or intravenous (IV)-drug abuse should be tested for syphilis, and all sexually active persons with syphilis should be tested for HIV (with the informed consent of the

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patient). HIV test results are clinically important in managing patients with syphilis and, with appropriate confidentiality safeguards, should be made available to medical personnel who care for these patients.

2. When clinical findings suggest syphilis is present, but serologic tests are negative, other tests should be used to determine if syphilis is present. These tests include dark-field microscopy and direct fluorescent antibody for *T. pallidum* (DFA-TP) staining of lesion exudate and examination of biopsy tissue using DFA-TP or Steiner stain (*4*).†
3. Laboratories should titrate nontreponemal tests to a final endpoint, rather than reporting results as greater than an arbitrary cutoff (e.g.,>1:512). Specific results permit more accurate determination of response to therapy and also help identify unusual serologic responses to syphilis.
4. Neurosyphilis should be considered in the differential diagnosis of neurologic disease in HIV-infected persons.
5. Consultation should be obtained to evaluate unusual serologic test results in patients suspected of having syphilis or in those being followed for response to treatment.

Treatment and Follow-Up

Case reports have suggested that treatment failures, including progression to neurosyphilis, may occur more frequently in patients coinfected with HIV than in those with syphilis alone (*5,6*). This has not yet been confirmed, but because an intact cellular immune response is important in the host response to *T. Pallidum* infection (*7*) and because HIV infection impairs cellular immune response in some patients, an increased frequency of treatment failure is plausible.

Recommended treatment schedules for neurosyphilis have included benzathine penicillin (*8*), although treatment with benzathine penicillin in currently recommended dosages does not achieve treponemicidal antibiotic levels in the cerebrospinal fluid (CSF) of most patients with syphilis, and treatment failures have been reported (*9–11*).

Recommendations

1. No change in therapy for early syphilis for HIV-coinfected patients is recommended. However, there is disagreement on this issue, and some authorities have advised CSF examination and/or treatment with a regimen appropriate for neurosyphilis for all patients coinfected with syphilis and HIV, regardless of the clinical stage of syphilis (*12*). In all cases, careful follow-up is necessary to assure adequacy of treatment.
2. Serologic testing after treatment for early syphilis is important for all patients, regardless of HIV infection status. In patients coinfected with HIV, quantitative nontreponemal tests should be repeated at 1, 2, and 3 months and at 3-month intervals thereafter until a satisfactory serologic response to treatment occurs. If the titer does not decrease appropriately (two-dilution decrease by 3 months for primary syphilis or by 6 months for secondary syphilis) (*13*) or if a sustained two-dilution or greater increase occurs, the patient should be reevaluated to consider the possibility of treatment failure or reinfection, and CSF should be examined. Sexually transmitted disease (STD) clinics and others providing STD treatment should assure adequate follow-up.
3. A CSF examination should precede and guide treatment of HIV-infected patients with latent syphilis present for longer than 1 year or for unknown duration. If an examination is not possible, patients should be treated for presumed neurosyphilis.
4. Benzathine penicillin regimens should not be used to treat either asymptomatic or symptomatic neurosyphilis in HIV-infected patients. Patients should be treated for at least 10 days with either aqueous crystalline penicillin G, 2–4 million units IV every 4 hours (12–24 million units each day), or aqueous procaine penicillin G, 2.4 million units intramuscularly daily, plus probenecid 500 mg orally 4 times daily (*8*).

Reported by: Div of Sexually transmitted Diseases, Center for Prevention Svcs; AIDS Program and Sexually Transmitted Diseases Laboratory Program, Center for Infectious Diseases, CDC.

Editorial Note: The expert consultants also highlighted the following research priorities related to the diagnosis and treatment of syphilis in HIV-coinfected patients:

1. The effect of HIV infection on initial clinical and laboratory manifestations of syphilis and on the efficacy of current syphilis therapy should be prospectively studied.
2. A surveillance system should be developed to detect complications of syphilis, especially neurosyphilis, and unusual clinical and laboratory manifestations of syphilis in patients with and without HIV-coinfection.
3. The importance of CNS involvement in early syphilis should be determined in patients with and without HIV coinfection.
4. Better laboratory methods should be developed for detecting *T. pallidum* or *T. pallidum* antigens in CSF, blood, and lesions.
5. A better animal model of *T. pallidum* infection is needed to examine the effect of immunosuppression on the course of syphilis.

So that the frequency of unusual manifestations of syphilis can be determined, health-care providers are requested to notify their state epidemiologists of HIV-infected patients who meet one of the following conditions:

1. Neurosyphilis confirmed by CSF examination or histopathology;
2. Negative serologic tests for syphilis (nontreponemal [VDRL, RPR] or treponemal [FTA-ABS, MHA-TP, HATTS] tests) during secondary syphilis diagnosed by darkfield microscopy or histopathology of lesion material.

The state epidemiologists will forward these reports without personal identifiers to the Division of Sexually Transmitted Diseases, Center for Prevention Services, CDC.

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†*In evaluating biopsy specimens, histologic stains (Warthin Starry Silver, Steiner) must be interpreted with caution since other spirochetes and artifacts may be misidentified as T. pallidum* with these silver stains.

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Reprinted from MMWR 1988;37:600-2, 607–8.

Update: Influenza Activity

Update

In 1988, influenza-like illness worldwide has been associated with all three virus types—A(H3N2), A(H1N1) and B. Different viruses predominated in different countries.

Oceania. In New Zealand, where influenza activity has been greater than in recent years, activity began in April and peaked in June. Virus isolates have been almost exclusively type A(H3N2). Persons of all ages have been infected, and one influenza-associated death has been confirmed. In Australia, type A(H1N1) virus predominated; in western Australia, type A(H3N2) virus has also been isolated. In Fiji, outbreaks of influenza type A(H1N1) during August were reported.

Asia. In June, outbreaks of influenza A(H1N1) occurred among schoolchildren in southern China. In addition, Hong Kong and Singapore reported sporadic cases of all types of influenza in children and adults. The Republic of Korea, which reported outbreaks of all types of influenza in Seoul earlier this year, has reported only sporadic cases since April. Taiwan, where type B virus was reported early in the year, reported localized outbreaks of type A(H1N1) virus in June and July.

South America. Chile and Uruguay have reported widespread influenza A(H3N2) activity that began in May and peaked in June. In Uruguay, influenza B was also isolated in June. Argentina and Panama reported influenza type B isolates from June through August; however, since mid-September, Panama has reported serologically confirmed influenza A(H3N2). Viral isolations are pending.

Europe and United States. Influenza has been isolated in Europe and the United States throughout the summer. England reported an outbreak of influenza A(H3N2) among young men in a military unit in July, and Czechoslovakia reported type A(H1N1) virus activity in June. In the United States, influenza B isolates were reported from Arizona during June, July, and August and from Texas in late July. Type A(H1N1) virus was isolated from a child with non-Hodgkin's lymphoma in Washington, D.C., in late July.

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Cases of selected notifiable diseases, Virginia, for the period October 1, through October 31, 1988.

Disease	State					Regions				
			Total to Date		Mean 5 Year To Date	This Month				
	This Month	Last Month	1987	1988		N.W.	N.	S.W.	C.	E.
Measles	34	23	1	200	23	0	0	34	0	0
Mumps	15	0	73	134	41	0	7	6	1	1
Pertussis	0	2	49	21	34	0	0	0	0	0
Rubella	0	0	1	11	1	0	0	0	0	0
Meningitis—Aseptic	43	26	241	149	256	10	12	1	5	15
*Bacterial	23	7	148	139	191	4	2	6	2	9
Hepatitis A (Infectious)	33	23	207	326	130	2	8	0	3	20
B (Serum)	34	29	365	273	428	1	5	10	4	14
Non-A, Non-B	10	3	44	67	65	0	2	2	1	5
Salmonellosis	310	228	1616	1516	1313	34	85	56	81	54
Shigellosis	56	29	190	394	137	4	14	5	10	23
Campylobacter Infections	105	56	516	578	526	23	21	19	17	25
Tuberculosis	31	36	371	333	360	1	3	4	8	15
Syphilis (Primary & Secondary)	46	50	267	363	333	0	6	3	21	16
Gonorrhea	1318	1643	12467	11943	15785	—	—	—	—	—
Rocky Mountain Spotted Fever	3	2	19	18	40	0	0	1	0	2
Rabies in Animals	24	32	316	308	278	7	4	1	8	4
Meningococcal Infections	3	2	62	46	59	0	1	1	0	1
Influenza	8	1	1265	2447	1653	0	0	0	0	8
Toxic Shock Syndrome	0	1	1	1	6	0	0	0	0	0
Reye Syndrome	0	0	0	0	3	0	0	0	0	0
Legionellosis	1	3	8	10	18	0	0	1	0	0
Kawasaki's Disease	1	0	21	12	24	0	0	1	0	0
Acquired Immunodeficiency Syndrome	26	43	191	314	—	1	8	5	9	3

Counties Reporting Animal Rabies: Buckingham 1 cat; Caroline 1 skunk, 1 raccoon; Charles City 1 raccoon; Chesterfield 1 raccoon; Craig 1 raccoon; Cumberland 1 raccoon; Fairfax 1 cat, 2 raccoons; Goochland 1 fox; Henrico 2 raccoons; James City 2 raccoons, 1 skunk; Loudoun 1 raccoon; Northumberland 1 raccoon; Orange 1 skunk; Page 3 skunks; Rappahannock 1 skunk; Richmond City 1 raccoon.

Occupational Illnesses: Asbestosis 17; Loss of Hearing 11; Mesothelioma 1; Occupational Asthma 1; Pneumoconioses 37.

*other than meningococcal

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